IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Neil H. Bander
Serial No. : 09/357,704
Filed : July 20, 1999
Title : TREATMENT AND DIAGNOSIS OF PROSTATE CANCER

Art Unit : 1642
Examiner : Gary B. Nickol

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BRIEF ON APPEAL

Appellant is appealing the final rejection of claims 69-80, 124-127, 129, 130, 136-173 and 186-189 dated July 9, 2004. A Notice of Appeal was mailed on August 13, 2004.

(1) Real Party in Interest

The Real Party in Interest is Millennium Pharmaceuticals, Inc., 40 Landsdowne Street, Cambridge, Massachusetts 02139. Millennium Pharmaceuticals, Inc. is the exclusive licensee of the above-identified application from the assignee, Cornell Research Foundation.

(2) Related Appeals and Interferences

The present appeal is related to appeals filed, or soon-to-be filed (in the case of 09/929,665), in the following copending applications:

USSN 09/357,710;
USSN 09/357,709;
USSN 09/929,546; and
USSN 09/929,665.

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

2/15/05
Date of Deposit

Signature

Alissa Passacantilli
Typed or Printed Name of Person Signing Certificate

(3) Status of Claims

Claims 69-80, 124-127, 129, 130, 136-173 and 186-189 are pending and presented in the Claims Appendix.

Claims 69-80, 124-127, 129, 130, 136-173 and 186-189 are rejected under 35 U.S.C. § 112, first paragraph.

Claims 187-189 were canceled in an Amendment After Final dated August 13, 2004. Claims 69-70, 72-80, 124, 129, 130, 136-159, 164, 166-173 and 186 were amended in the Amendment After Final dated August 13, 2004. The majority of the amendments were to correct minor typographical errors. The remainder were made to obviate the Examiner's rejection under 35 U.S.C. §112, first paragraph regarding the "scope of enablement for reasons of record with regards to prevention of prostate cancer."

Claims 69-80, 124-127, 129, 130, 136-173 and 186-189 are being appealed. However, Appellant notes that if the claim cancellations in the Amendment After Final dated August 13, 2004 are acknowledged and entered, claims 69-80, 124-127, 129, 130, 136-173 and 186 are being appealed.

(4) Status of Amendments

All of the amendments filed in this case have been entered except for the Amendment After Final filed August 13, 2004. Appellant asks that the amendments to the claims and the cancellation of claims as provided in the Amendment After Final dated August 13, 2004 be entered as they either correct minor typographical errors or reduce the number of issues on appeal.

(5) Summary of Claimed Subject Matter

One aspect of the claimed invention features a method of treating, or preventing or delaying progression of prostate cancer that comprises: providing an antibody or antigen binding portion thereof which competes for binding to prostate specific membrane antigen (PSMA) with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody; and administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat, or prevent or delay the progression of prostate cancer.

Support can be found, e.g., at page 9, line 28 through page 10, line 16; page 13, line 11 through page 14, line 10; page 19, lines 20-36; and page 27, line 26 through page 28, line 10 of the specification.

In another aspect, the claimed invention features a method of treating, or preventing or delaying progression of prostate cancer that comprises: providing an antibody or antigen binding portion thereof which competes for binding to prostate specific membrane antigen with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody, wherein the antibody is labeled with the radiolabel ^{90}Y; and administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat or prevent or delay the progression of prostate cancer. Support can be found, e.g., at page 9, line 28 through page 10, line 16; page 13, line 11 through page 14, line 10; page 19, lines 20-36; page 27, line 26 through page 28, line 10 of the specification; and page 28, lines 27-28.

Another aspect of the claimed invention features a method of treating, or preventing or delaying progression of prostate cancer that comprises: providing an antibody or antigen binding portion thereof which competes for binding to prostate specific membrane antigen with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody, wherein the antibody is labeled with a radiolabel, and wherein the radiolabel is a beta- or gamma-emitter; and administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat, or prevent or delay the progression of prostate cancer. Support can be found, e.g., at page 9, line 28 through page 10, line 16; page 13, line 11 through page 14, line 10; page 19, lines 20-36; page 27, line 26 through page 28, line 10 of the specification; and page 28, lines 27-28.

In another aspect, the claimed invention features a method of treating, or preventing or delaying progression of prostate cancer that comprises: providing an antibody or antigen binding portion thereof which competes for binding to prostate specific membrane antigen with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody, wherein the antibody is bound to a cytotoxic drug of bacterial origin; and

administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat, or prevent or delay the progression of prostate cancer. Support can be found, e.g., at page 9, line 28 through page 10, line 16; page 13, line 11 through page 14, line 10; page 19, lines 20-36; page 27, line 26 through page 28, line 10 of the specification; and page 26, lines 18-22.

Another aspect of the claimed invention features a method of treating, or preventing or delaying progression of prostate cancer that comprises: providing an antibody or antigen binding portion thereof which competes for binding to prostate specific membrane antigen with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody, wherein the antibody is bound to a cytotoxic drug of plant origin; and administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat, or prevent or delay the progression of prostate cancer. Support can be found, e.g., at page 9, line 28 through page 10, line 16; page 13, line 11 through page 14, line 10; page 19, lines 20-36; page 27, line 26 through page 28, line 10 of the specification; and page 26, lines 18-22.

(6) Grounds of Rejection

Claims 69-80, 124-127, 129-130, 136-173 and 186-189 stand rejected under 35 U.S.C. §112, first paragraph, "scope of enablement ... with regards to the prevention of prostate cancer."

Claims 69-80, 124-127, 129-130, 136-173 and 186-189 stand rejected under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the invention."

(7) Argument

Enablement

Claims 69-80, 124-127, 129-130, 136-173 and 186-189 stand rejected under 35 U.S.C. §112, first paragraph, "scope of enablement for the reasons of record with regards to the prevention of prostate cancer."

As discussed above, Appellant has amended the claims in the Amendment After Final filed August 13, 2004 to remove language regarding the "prevention" of prostate cancer, thereby obviating this rejection. Appellants request that this amendment be entered to thereby reduce the number of issues on appeal in the above-identified application.

Written Description

Claims 69-80, 124-127, 129, 130, 136-173, 186 and 190 are rejected under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the invention." The Examiner argued that although there was support for a broader genus, and for various species, there was no support for the claims. Specifically, the Examiner asserts that:[1]

> "the written description is not commensurate in scope with the claims drawn to an antibody or antigen binding portion thereof which **competes for binding** to prostate specific membrane antigen (PSMA) with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody." (emphasis in the original)

Thus, the sole issue is whether the specification and claims as filed provide written description support for the claim term "competes for binding to prostate specific membrane antigen with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody." This phrase is often referred to herein as the "disputed claim term." No other element of the claims was said to lack written description.

---

[1] See page 3, first paragraph, of the Final Office Action of July 9, 2004.

Appellant respectfully traverses the rejection.

The case law sets forth at least three ways that written description support for claimed subject matter can be shown. These are *in haec verba* support, explicit support and inherent (or implicit) support. *In haec verba* and explicit support are often referred to as forms of express support. *In haec verba* support comes from language in the specification that identically recites the claimed subject matter. Explicit support is derived from language that while not identical to the language in the claim, is equivalent thereto. Lastly, where express language is lacking, support may be found either inherently (or implicitly) in the specification. See, e.g., MPEP 2163(I) and MPEP 2163 (II)(A)(b).

As provided in the responses filed on August 13, 2004[2], and April 12, 2004, and as set forth below, the instant application provides explicit and/or implicit written description support for the disputed claim term. This is not a situation were support needs to be implied from the disclosure of a genus and/or species. Therefore, there is no need to rely on case law regarding implicit support. However, even if it is argued that there is no explicit support (which is not the case), the specification provides inherent or implied written description support for the disputed claim term. We turn now to Appellant's arguments.

The specification provides explicit support for the disputed claim term

The written description requirement is met if the specification shows that an applicant was in possession of the claimed invention at the time of filing. "When the original specification accomplishes [this], regardless of *how* it accomplishes it, the essential goal of the description requirement is realized." *In re Smith*, 481 F.2d 910, 914, 178 USPQ 620 (CCPA 1973). It is well accepted that "in order to satisfy the written description requirement, the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue." *Purdue Pharma v. Faulding, Inc.*, 230 F.3d 1320, 56 USPQ 2d 1481 (Fed. Cir. 2000); and MPEP § 2163.02. As provided, for example, in *In re Wright*, 866 F.2d 422, 9 USPQ2d 1649 (Fed. Cir. 1989), "the fact...that the exact words here in question...are not in the specification is not important." See also MPEP 2163.02, "The subject matter of the claim need not be described

[2] The after final response filed on August 13, 2004, included a Declaration of Abbie Celniker under 37 CFR § 1.132. Similar versions of this Declaration have been cited and entered in the co-pending applications on appeal.

literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement." and MPEP 2163 (I)(B), "While there is no *in haec verba* requirement, newly added claim language must be supported in the specification through express, implicit, or inherent disclosure."

The analysis in the Final Office Action begins with a discussion of a passage in the specification which concerns the use of competing and non-competing antibodies in the preparation of prodrug/activator systems.[3] Most, if not all, of the arguments made in the Final Office Action center on this passage. Appellant will first discuss the relevance of the passage to written description of the disputed claim term and then go on to discuss the analysis in the Final Office Action which relate to the passage.

The specification as a whole is directed to anti-PSMA antibodies, to methods of making such antibodies, and to a variety of uses to which such antibodies can be put. One disclosed use of antibodies of the disclosure is as starting materials for use in the construction of antibody-prodrug conjugates and antibody-prodrug activator conjugates. Two classes of antibodies of the invention, competing and non-competing, are described in the section on the selection of antibodies as starting materials for use in making the conjugates.[4] The passage referred to above provides as follows:

> a first biological agent[5] is conjugated with a prodrug which is activated only when in close proximity with a prodrug activator. The prodrug activator is conjugated with a second biological agent <u>according to the invention</u>, preferably one which binds to a non-competing site on the prostate specific membrane antigen molecule. Whether two biological agents bind to competing or non-competing binding sites can be determined by conventional competitive binding assays. (emphasis added)

Thus, the passage, alone or in combination with the rest of the specification, explicitly discloses two types of antibodies:

---

[3] See page 27, lines 27-35, of the specification.
[4] See page 27, lines 27-35, of the specification.
[5] Biological agent are discussed as follows at page 13, lines 14-19, "The process involves providing a biological agent, such as an antibody or binding portion thereof, probe, or ligand, which binds to an extracellular domain of prostate specific membrane antigen of (i.e., a portion of prostate specific membrane antigen which is external to) such cells."

1. Antibodies that compete for binding with an antibody according to the invention; and

2. Antibodies that do not compete for binding with an antibody according to the invention.

The passage also provides that non-competing antibodies are preferred in one embodiment and that non-competing antibodies should, in that embodiment, be distinguished from competing antibodies. The text also provides, see, e.g., the last sentence of the quoted passage, what constitutes a competing biological agent and a non-competing biological agent by stating that "whether two biological agents bind to competing or non-competing sites can be determined by conventional competition binding assays." So, whether preferred or not for use in this particular application (prodrug/prodrug activator systems), it is clear the text explicitly describes antibodies which compete with an antibody of the invention. The effort the inventor went to in order to characterize the two different classes of antibodies, and the very recognition of the necessity of avoiding the competing class in a preferred conjugate construct, shows that the inventor was in possession of the concept of competing antibodies. Thus, a person of ordinary skill in the art at the time the application was filed could reasonably conclude that the inventor was in possession of the concept of having "an antibody that competes for binding with an antibody according to the invention."

All that remains is to show support for the concept that the antibody "according to the invention" referred to in the cited language above can be one of the antibodies recited in the claims, namely E99, J415, J591 or J533. Antibodies E99, J415, J533 and J591 are disclosed throughout the specification as being antibodies of the invention. They are the only species described in the specification. In fact, the very next sentence[6] after the passage recited above is as follows:

> For example, monoclonal antibodies J591, J533, and E99 bind to competing binding sites on the prostate specific membrane antigen molecule. Monoclonal antibody J415, on the other hand, binds to a binding site which is non-competing with the site to which J591, J533, and E99 bind.

[6] See page 28, lines 1-6, of the specification.

Upon reviewing the specification one of ordinary skill at the time the application was filed, could have reasonably concluded that monoclonal antibodies E99, J415, J533 and J591 are "antibodies according to the invention."

Given that the specification clearly supports the concept of "antibodies that compete for binding with an antibody of the invention," and that J415, J591, J533 and E99 are each antibodies of the invention, a skilled artisan could reasonably conclude that that the inventor was in possession of the disputed claim term, namely "competes for binding to prostate specific membrane antigen with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody" at the time of filing.

We turn now to the analysis in the Final office Action of the passage discussed above. The analysis does the following:

it improperly ignores the plain language of the passage which explicitly describes antibodies which compete with an antibody of the invention;

it takes the incorrect position that the cited passage must be read in isolation from the rest of the specification and that the cited passage only provides written description for antibodies which can be used in prodrug/activator systems and that to do otherwise is to take the support "out of context";

it takes the incorrect position that competing antibodies will not work in such systems;

it is based, at least in part, on a misinterpretation of the law, namely that there can only be written description for antibodies that work in prodrug/activator systems; and

it comes to the erroneous conclusion that there is no written description support for the disputed claim term. If any element of this argument fails the entire argument falls. In fact, as set out below, each of the elements of this analysis is fatally flawed.

The analysis in the Final Office Action begins by ignoring both the specification as a whole, which is very largely devoted to anti-PSMA antibodies, and the plain language of the cited passage.

The analysis then goes on to erect an intricate analytical framework, by first arguing that the support for the disputed claim term has been taken out of context in the Appellant's

arguments. In response to the Appellant's remarks about the passage[7] discussed earlier herein the Final Office Action provides the following argument:[8]

> This argument has been considered but is not found persuasive as it appears that the alleged support has been taken out of context. The passage that applicants refer to pertains to biological agents conjugated to prodrugs- such as antibody conjugates.

The Final Office Action argues that the passage relates only to antibodies which are conjugated to the prodrug or activator (see his emphasis on the word conjugated). A review of the specification as a whole, and of the cited passage, shows that this interpretation is far too restrictive. The entire specification is directed to anti-PSMA antibodies and to methods of making such antibodies, and to a variety of uses to which such antibodies can be put. As discussed above, the cited passage describes particular classes of antibodies of the invention, competing and non-competing, in connection with selecting starting materials for use in making the conjugates. There is simply no support in the specification for the position that the classes of competing and non-competing antibodies have no existence outside the use in a prodrug/activator conjugate. The two classes of antibody exist independently of the prodrug system.

The analysis in the Final Office Action goes on as follows:[9]

> Prodrugs are inactive drugs. In the instant case, the conjugated prodrug becomes activated (page 27, line 28) "only when in *close* proximity with a prodrug activator". Thus, the fact that a preferred embodiment of a prodrug/prodrug activator scenario is one in which the biological agent binds in close proximity to one another (i.e...to non-competing sites) on the antigen is not surprising given the fact that said activators must be nearby to activate the prodrug. In contrast, however, it would be surprising and quite complex to conceive of administering biological agents conjugated to prodrugs and or prodrug activators that bind *competing* sites on the antigen because such sites are indicative of the same epitope. Hence the administration of biological agents (for the purposes of activating a prodrug) that bind to competing sites would effectively reduce the probability that a prodrug would be activated. Thus, applicants alleged support for the inclusion of "competing" sites is not found persuasive because there is no contextual nexus that adequately provides support for the newly amended claims.

---

[7] Reproduced on page 7 herein and found at page 27, lines 27-35, of the specification.
[8] See page 4, first full paragraph, of the Final Office Action of July 9, 2004.
[9] See page 4, first full paragraph, of the Final Office Action of July 9, 2004.

In this section, the analysis argues that competing antibodies will not work in a prodrug/activator system, that only antibodies that work in a conjugate have written description, and therefore there is no written description of competing antibodies. The reasoning is based on a misinterpretation of the specification, on factual error or unfounded speculation, and on misapplication of the law.

First, the passage is misinterpreted. It does not limit prodrug/activator systems to those using non-competing antibodies. The passage on antibody selection for prodrug applications merely says that non-competing antibodies are preferred—it by no means rules out the use of competing antibodies. The inventor could have used more restrictive language, e.g., he might have said "competing antibodies are not suitable for use in prodrug/activator systems" but he did not do so.

Furthermore, the analysis is based on unfounded assumptions or factual error about the prodrug/activator system. No reasonable basis is presented to support the view that despite the plain language in the cited passage, a competing antibody would not work in a prodrug/activator system. The passage discloses the need for close proximity of the prodrug and activator. The Final Office Action argues that the recited close proximity is equivalent to non-competing sites (see the language in the Final Office Action that reads as follows, "close proximity to one another (i.e...to non-competing sites[10])." There is nothing in the application or of record, other than the speculation or unsubstantiated conclusion made in the Final Office Action, that suggests that an antibody would have to bind a non-competing site on an antigen to be "in close proximity." E.g., competing antibodies that bind to overlapping epitopes, in the process of competing one another off and on the antigen, might just as well create the needed close proximity between the prodrug coupled to one of the competing antibodies and the activator coupled to another competing antibody. A prodrug activator conjugate might just as well activate a prodrug conjugate by binding an epitope on a first PSMA antigen located "in close proximity" to a second PSMA antigen that is bound by the prodrug conjugate at the same epitope on the second PSMA antigen (PSMA is found as a dimer on cells).

[10] See the second sentence of the language in the Final Office Action reproduced at page 10 above.

Finally, the rejection is based on a misinterpretation of the law. The analysis in the Final Office Action relies heavily on the argument that prodrug/activator systems made with competing antibodies will not work. See the text of the arguments quoted above, especially the segment which reads as follows, "... it would be surprising and quite complex to conceive of administering biological agents conjugated to prodrugs and or prodrug activators that bind *competing* sites on the antigen because such sites are indicative of the same epitope." The analysis confuses the utility or enablement of a prodrug/activator system (which is not the subject of the claims) with written description of the antibody components used to make the prodrug/activator system. The analysis assumes that a prodrug/activator system which uses competing antibodies will not work or could not be made to work without undue experimentation. Even if that were true it would go to the issue of whether claims to a prodrug/activator system made with competing antibodies would have utility or would be enabled, and not to the issue of whether there is written description for the antibodies used to make the conjugate. [11]

Thus, the argument in the Final Office Action is flawed at every stage. To summarize:

First, it ignores the plain language of the cited passage which explicitly describes competing antibodies. Quite simply, the passage provides explicit support for competing antibodies so the argument in the Final Office Action falls once one looks to this language. The analysis is wrong and as such the rest of the arguments are moot.

Next, without any support, it is concluded that the classes of antibody explicitly described must be interpreted as having an existence only in relationship to prodrug/activator systems. There is absolutely no basis for this. The analysis is wrong and as such the rest of the arguments, which depend on this, are moot.

Next, the Final Office Action argues that competing antibodies will not work in such systems. This is based on a misreading of the passage and unwarranted assumptions or factual error with regard to the types of antibodies which can be used in the conjugates.

Finally, the Final Office Action argues that there can only be written description for antibodies that work in prodrug/activator systems. Here, the analysis confuses utility or

[11] This is not Appellant's position. Appellant does not take the position that any particular prodrug/activator system lacks utility or is not enabled.

enablement of conjugates with written description of the antibodies. Even if the analysis were right on the enablement or utility of the conjugate, it would not defeat written description of the antibodies.

Perhaps the most important flaw in the arguments made in the Final Office Action is that they never address the issue of why there is no express support for the disputed term, despite the plain explicit language in the specification. Instead, the analysis centers on an intricate multistage analysis that is irrelevant and/or flawed at every stage. The PTO has not met the burden of showing that the written description of the claims is lacking.

The Final Office Action then provides further discussion of the mechanism of binding, the fact that the passage prefers non-competing antibodies, and the fact that examples of non-competing antibodies are given.[12] The examples of what can be used in a preferred embodiment are just that—examples of a preferred use. This is simply more of what Appellant has addressed above. It is irrelevant and flawed for the same reasons.

To accept the position provided in the Final Office Action on written description would mean accepting the position that the specification must provide *in haec verba* description. That is not the law. The arguments in the Final Office Action ignore the teaching of the application as a whole and ignore the plain language of the passage discussed in detail above. Instead, it relies on arguments that are irrelevant and/or flawed at every stage to thereby come to the conclusion that there is no express support. Appellant turns now to the issue of implicit support.

The specification provides implicit support for the disputed claim term

Even if it is argued that there is no explicit support for the disputed claim term, there is implicit written description support for it. The MPEP and the case law allow for inferring a sub-genus from other disclosure when the facts support doing so. *In re Smith*, 458 F.2d 1389, 173 USPQ 679 provides that "precisely how close the description must come to comply with section 112 must be left to case-by-case development ... it cannot be said that a sub-genus is necessarily always implicitly described by a genus encompassing it and a species upon which it reads." *In re Smith (1972)* does not enunciate a hard and fast rule that a genus and/or species cannot support a

[12] See pages 4 and 5 of the Final Office Action of July 9, 2004.

sub-genus. Instead, the determination must be made on a case-by-case basis. See, e.g., MPEP 2163(II)(A)(3)(b), which, citing *In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, provides:

> "[W]here no explicit description of a generic invention is to be found in the specification mention of representative compounds may provide an implicit description upon which to base generic claim language".

MPEP 2163.05 (II) refers to two cases which dealt with finding support for a sub-genus from generic and species disclosure, *In re Lukach,* 442 F.2d 967, 169 USPQ 795 (CCPA 1971) and *E parte Sorenson*, 3 U.S.P.Q.2d 1462 (Bd. Pat. App. & Interf. 1987).

In *In re Lukach*, the applicant argued that it was entitled to a sub-generic claim to a specific (narrow) range of molecular weight, namely 2.0-2.6. The applicant reasoned that because the disclosure included a broader genus range and a single species which inherently fell into the specific narrower sub-generic range (the sole species had a molecular weight of 2.6), it should be allowed to narrow the generic claim to the narrower specific sub-generic range. The applicant, relying largely on *In re Risse*, 378 F.2d 948, 154 USPQ 1 (1967) (which was at least partially overturned later), argued that support for a sub-genus required nothing more than the disclosure of a broader genus which wholly encompasses the questioned sub-genus and disclosure of a single species within the new sub-genus. The court found that even if the applicant's reliance on *In re Risse* was appropriate, there was no disclosure of the broader genus range. The court reasoned that a single species example of 2.6, alone, with nothing else in the specification or art pointing to the range, would not support a range of 2.0-2.6.

In *Ex parte Sorenson* the original application disclosed a broad genus of "copper complexes of carboxylic acids" as well as a number of species. Five working examples were from the originally unclaimed sub-genus of "binuclear copper complexes of carboxylic acids." Four of these working examples were from the sub-sub-genus of "binuclear copper complexes of aryl carboxylic acids" and one was from the sub-sub-genus of "binuclear copper complexes of alkyl carboxylic acids." The applicant sought to add a claim to the sub-genus, as well as to the two sub-subgenera. The examiner rejected the added sub-generic and sub-sub-generic claims for lack of implicit written description. The Board, reversed, relying in part on *In re Kalsow*, 707

F.2d 1366, 217 USPQ 1089 (Fed. Cir. 1983), for the proposition that the test is whether the originally filed specification reasonably conveys to a person of ordinary skill that the applicant had possession of the subject matter.

The instant case, when viewed from the perspective of implicit support, concerns the sufficiency of the written description of a sub-genus—"an antibody (or binding fragment) which competes with one of J591, E99, J415 and J533." This is referred to below as the "disputed sub-genus." One important consideration in *In re Lukach* and *Ex parte Sorenson* was the whether there was disclosure of a broader genus and a disclosure of species which would fall under the disputed sub-genus. Another critical consideration in analyzing the specification for support was whether anything in the specification pointed to the questioned sub-genus. Therefore, Appellant begins the analysis with a review of such disclosure in the specification.

The specification discloses the following genus, sub-genera (the disputed sub-genus is shown in brackets), and species, arranged in order of descending scope:

- A broad genus of all antibodies that bind to the extracellular domain of PSMA.[13] The Examiner has admitted that the specification describes this genus.[14]
- A relatively broad sub-genus of competing antibodies, i.e., all competing antibodies, which is broader than the disputed sub-genus.[15]
- [Antibodies that compete with J591, E99, J415 and J533]
- A relatively narrow sub-genus of competing antibodies, i.e., the sub-genus of J591, E99, and J533, which is narrower than the disputed sub-genus.[16]
- Four species J591, E99, J415 and J533.[17] The Examiner has admitted that the specification describes these species.[18] These species fall within the broad genus and the relatively broad sub-genus of competing antibodies. Several of them fall within the relatively narrow sub-genus of competing antibodies. They all fall within the disputed sub-genus of

[13] See page 16, lines 22-27, of the specification.
[14] See page 3, first full paragraph, of the Final Office Action of July 9, 2004.
[15] See page 27, lines 27-35, of the specification.
[16] See page 28, lines 1-3, of the specification.
[17] See page 35, lines 44-46, of the specification.
[18] See page 3, first full paragraph,, of the Final Office Action of July 9, 2004.

competing antibodies.[19] They are fully representative of the genus. The species share structural and functional homology but are representative of the sub-genus, some compete with one another while one does not.

Thus, the disputed sub-genus is bracketed by explicit disclosure in the specification. The broad genus, and the relatively broad sub-genus of competing antibodies, are broader than the disputed sub-genus. The relatively narrow sub-genus of competing antibodies, and the species, are narrower than the disputed sub-genus. In this respect, namely the presence of a broader taxa, the facts in the instant case are far more like those in *Ex parte Sorenson*, where support was found. The facts are even stronger here, as there are two broader genera, the genus and the relatively broad sub-genus of competing antibodies. The relatively narrow sub-genus of competing antibodies and the species are narrower than the disputed sub-genus. Again the facts in the instant matter are far more like those in *Ex parte Sorenson*, where support was found. Here there are four representative species, all of which are within the disputed sub-genus, wherein in *In re Lukach*, where support was not found, there was only one. And again, the facts are even stronger here than in *Ex parte Sorenson*, by virtue of the disclosure of the relatively narrower sub-genus of competing antibodies.

In *Ex parte Lukach*, the court relied very heavily on the lack of other disclosure pointing to the questioned sub-genus in reaching its finding of no support for the questioned sub-genus. Such guiding disclosure is referred to in some cases as blaze marks.[20, 21]

There is a wealth of guiding disclosure in the specification pointing to the disputed sub-genus. The amount of guiding disclosure found in the instant specification stands in stark contrast to what was found in *Ex parte Lukach*, where the court failed to find support. In the

---

[19] All of the disclosed antibodies not only define the scope of the claim (by specifying what an antibody must compete with to be within the claim) but are also within the disputed sub-genus. The fact that use of any one of the specified antibodies would infringe the claim shows they are all within the disputed sub-genus.

[20] The case law has recognized the importance of blaze marks or other disclosure which reasonably leads to the species or genus in question in determining if there is implicit support for a species or genus (in this case sub-genus), see e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 39 USPQ2d 1895 (Fed. Cir. 1996 In re Ruschig, 379 F.2d 990, 994-95, 154 USPQ 118 (CCPA 1967).

[21] The arguments in the Final Office Action might be construed to say that the broader sub-genus of competing antibodies is not described in the specification. Appellant's arguments concerning the description of that sub-genus were presented above, under the discussion of explicit support, and are incorporated here as well. The analysis in the Final Office Action is wrong on that count. But even if the broader sub-genus of competing antibodies were not described, the narrower sub-genus of competing antibodies is still there, pointing the way to the disputed sub-genus.

instant specification it is clear that sub-genera of competing antibodies of varying scope were disclosed (the relatively broad sub-genus of competing antibodies and the relatively narrow sub-genus of competing antibodies). These sub-genera of competing antibodies point the way to genera of competing antibodies of differing scope. Furthermore, the narrower sub-genus of competing antibodies (which is limited to J591, J533, and E99) points to the use of working examples disclosed in the specification to define the scope of a sub-genus of competing antibodies. The specification describes four, and only four, working examples, J591, E99, J415 and J533. This points the way to this important set of antibodies for use in defining the scope of the disputed sub-genus. There are no species one is forced to overlook or exclude. The guidance so critically lacking in *Ex parte Lukach* is found in the instant specification. The guidance found in the specification points clearly to a sub-genus of competing antibodies limited by being competitive with one of the four sole disclosed species, in other words, the disputed sub-genus.

Thus, the specification reasonably conveys that the inventor was in possession of a sub-genus of competing antibodies defined by these four important species, i.e., the disputed sub-genus, an anti-PSMA antibody which competes with any one of J591, E99, J415 and J533. Accordingly, even if there was no explicit support for the disputed claim term the specification provides implicit support for it.

Written description of a genus, whether support in the disclosure is *in haec verba*, explicit or implicit, also requires disclosure of a sufficient number of species. The Patent and Trademark Office's Revised Interim Written Description Guidelines Training Materials allows a single prophetic example of an antibody to support a genus where the antigen is well characterized. Here there is much more, there are four working examples, the antigen is well characterized, and the test for competition is well characterized. The species share structural and functional homology but are representative of the sub-genus, some compete with one another while one does not.

In summary, it is clear that the inventor was in possession of antibodies that compete for binding with E99, J591, J415 or J533. The rejection should be removed the case sent back to the Examiner for immediate allowance.

Respectfully submitted,

Date: February 15, 2005

Laurie Butler Lawrence
Reg. No. 46,593

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

21002468.doc

Appendix of Claims

69. A method of treating, or preventing or delaying progression of prostate cancer comprising:

providing an antibody or antigen binding portion thereof which competes for binding to prostate specific membrane antigen (PSMA) with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody; and

administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat, or prevent or delay the progression of prostate cancer.

70. The method according to claim 69, wherein the prostate cancer is metastatic.

71. The method according to claim 70, wherein the metastatic prostate cancer involves a bone marrow or a lymph node metastasis.

72. A method according to claim 69, wherein the administering is carried out parenterally.

73. A method according to claim 72, wherein the administering is carried out intravenously.

74. A method according to claim 69, wherein the administering is carried out by intracavitary instillation.

75. A method according to claim 69, wherein the administering is carried out rectally.

76. A method according to claim 69, wherein the antibody or antigen binding portion thereof is administered following a prostatectomy.

77. A method according to claim 69, wherein the antibody or antigen binding portion binds live cells.

78. A method according to claim 69, wherein the antibody is selected from the group consisting of a monoclonal antibody and a polyclonal antibody.

79. A method according to claim 78, wherein the antibody is selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody.

80. A method according to claim 78, wherein the antibody is a monoclonal antibody produced by a hybridoma having an ATCC Accession Number selected from the group consisting of HB-12101, HB-12109, HB-12127, and HB-12126.

124. A method of treating, or preventing or delaying progression of prostate cancer comprising:

providing an antibody or antigen binding portion thereof which competes for binding to prostate specific membrane antigen with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody, wherein the antibody is labeled with the radiolabel ^{90}Y; and

administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat or prevent or delay the progression of prostate cancer.

125. A method of treating, or preventing or delaying progression of prostate cancer comprising:

providing an antibody or antigen binding portion thereof which competes for binding to prostate specific membrane antigen with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody, wherein the antibody is labeled with a radiolabel, and wherein the radiolabel is a beta- or gamma-emitter; and

administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat, or prevent or delay the progression of prostate cancer.

126. A method of treating, or preventing or delaying progression of prostate cancer comprising:

providing an antibody or antigen binding portion thereof which competes for binding to prostate specific membrane antigen with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody, wherein the antibody is bound to a cytotoxic drug of bacterial origin; and

administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat, or prevent or delay the progression of prostate cancer.

127. A method of treating, or preventing or delaying progression of prostate cancer comprising:

providing an antibody or antigen binding portion thereof which competes for binding to prostate specific membrane antigen with a monoclonal antibody selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody, wherein the antibody is bound to a cytotoxic drug of plant origin; and

administering the antibody or antigen binding portion thereof to a subject under conditions effective to treat, or prevent or delay the progression of prostate cancer.

129. A method according to claim 69, wherein the antibody or antigen binding portion thereof competes for binding to prostate specific membrane antigen with monoclonal antibody J591.

130. A method according to claim 69, wherein the antibody or antigen binding portion thereof competes for binding to prostate specific membrane antigen with monoclonal antibody J415.

136. A method according to claim 69, 125, 126 or 127, wherein the antibody is a monoclonal antibody.

137. A method according to claim 69, 125, 126 or 127, wherein the antibody or antigen

binding portion thereof is internalized with the prostate specific membrane antigen.

138. A method according to claim 69, 125, 126 or 127, wherein the antibody or antigen binding portion thereof is selected from the group consisting of a Fab fragment, a F(ab')2 fragment, and a Fv fragment.

139. A method according to claim 69, wherein the antibody or antigen binding portion thereof further comprises a cytotoxic drug.

140. A method according to claim 139, wherein the cytotoxic drug is selected from the group consisting of a therapeutic drug, a compound emitting radiation, molecules of plant, fungal, or bacterial origin, biological proteins, and mixtures thereof.

141. A method according to claim 140, wherein the cytotoxic drug is a compound emitting radiation.

142. A method according to claim 141, wherein the compound emitting radiation is an alpha-emitter.

143. A method according to claim 142, wherein the alpha-emitter is selected from the group consisting of ^{212}Bi, ^{213}Bi, and ^{211}At.

144. A method according to claim 141, wherein the compound emitting radiation is a beta-emitter.

145. A method according to claim 144, wherein the beta-emitter is ^{186}Re.

146. A method according to claim 144, wherein the beta-emitter is ^{90}Y.

147. A method according to claim 141, wherein the compound emitting radiation is a

gamma-emitter.

148. A method according to claim 147, wherein the gamma-emitter is ^{131}I.

149. A method according to claim 141, wherein the compound emitting radiation is a beta- and gamma-emitter.

150. A method according to claim 140, wherein the cytotoxic drug is a molecule of bacterial origin.

151. A method according to claim 140, wherein the cytotoxic drug is a molecule of plant origin.

152. A method according to claim 140, wherein the cytotoxic drug is a biological protein.

153. A method according to claim 69, wherein the antibody or antigen binding portion thereof further comprises a label.

154. A method according to claim 153, wherein the label is selected from the group consisting of a biologically-active enzyme label, and a radiolabel.

155. A method according to claim 154, wherein the label is a radiolabel selected from the group consisting of ^{111}In, ^{99}mTc, ^{32}P, ^{125}I, ^{131}I, ^{14}C, ^{3}H and ^{188}Rh.

156. A method according to claim 69, 125, 126 or 127, wherein the antibody or antigen binding portion thereof is effective to initiate an endogenous host immune function.

157. A method according to claim 156, wherein the endogenous host immune function is complement-mediated cellular cytotoxicity.

158. A method according to claim 156, wherein the endogenous host immune function is antibody-dependent cellular cytotoxicity.

159. A method according to claim 69, 125, 126 or 127, wherein the antibody or antigen binding portion thereof is in a composition further comprising a pharmaceutically acceptable carrier, excipient, or stabilizer.

160. The method according to claim 69, 125, 126 or 127 wherein the antibody or antigen binding portion thereof is administered in conjunction with a second therapeutic modality.

161. The method according to claim 160, wherein the second therapeutic modality is selected from the group consisting of surgery, radiation, chemotherapy, immunotherapy and hormone replacement.

162. The method according to claim 161, wherein the hormone replacement comprises treatment with estrogen or an anti-androgen agent.

163. The method according to claim 162, wherein the anti-androgen agent is an agent which blocks or inhibits the effects of testosterone.

164. The method according to claim 126, wherein the prostate cancer is metastatic.

165. The method according to claim 164, wherein the metastatic prostate cancer involves a bone marrow or a lymph node metastasis.

166. A method according to claim 126, wherein the administering is carried out parenterally.

167. A method according to claim 166, wherein the administering is carried out

intravenously.

168. A method according to claim 126, wherein the administering is carried out by intracavitary instillation.

169. A method according to claim 126, wherein the administering is carried out rectally.

170. A method according to claim 126, wherein the antibody or antigen binding portion thereof is administered following a prostatectomy.

171. A method according to claim 126, wherein the antibody or antigen binding portion binds live cells.

172. A method according to claim 126, wherein the antibody is selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody.

173. A method according to claim 126, wherein the antibody is a monoclonal antibody produced by a hybridoma having an ATCC Accession Number selected from the group consisting of HB-12101, HB-12109, HB-12127, and HB-12126.

186. A method according to claim 126, wherein the antibody or antigen binding portion thereof competes for binding to prostate specific membrane antigen with monoclonal antibody J591.

187. A method according to claim 69, 124, 125, 126, or 127, wherein the method is a method of treating prostate cancer.

188. A method according to claim 69, 124, 125, 126, or 127, wherein the method is a method of preventing progression of prostate cancer.

189. A method according to claim 69, 124, 125, 126, or 127, wherein the method is a method of delaying progression of prostate cancer.